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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,929	09/28/2005	Larissa Vasilets	VASILETS 1 PCT	3688
25889	7590	10/02/2008	EXAMINER	
COLLARD & ROE, P.C. 1077 NORTHERN BOULEVARD ROSLYN, NY 11576			HURST, JONATHAN M	
			ART UNIT	PAPER NUMBER
			4153	
			MAIL DATE	DELIVERY MODE
			10/02/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/550,929	VASILETS, LARISSA	
	<b>Examiner</b>	<b>Art Unit</b>	
	JONATHAN M. HURST	4153	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-9 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_ is/are allowed.
- 6) Claim(s) 1-9 is/are rejected.
- 7) Claim(s) \_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 28 September 2005 is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. ____ .                                     |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|   | 6) <input type="checkbox"/> Other: ____ .                         |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :09/28/2005, 12/12/2005, and 07/27/2007.

## **DETAILED ACTION**

### ***Information Disclosure Statement***

1. The following documents, MANN, M. ET AL: "Analysis of protein phosphorylation using mass spectrometry: deciphering the phosphoproteome", YAN, Jun X. ET AL: "Protein phosphorylation: technologies for the identification of phosphoamino acids", WO 87/03095, DE 10051252, and WO 02/095058, cited in the information disclosure statement filed on 07/27/2007 have been already submitted and considered as part of the information disclosure statement filed on 09/28/2005
  
2. The following document, BRANDT, W., ANDERS, A. AND VASILETS, L.A. (2002) "Predicted alterations in Tertiary Structure of the N-terminus of the Na+/K+-ATPase  $\alpha$ -Subunit caused by Phosphorylation or Acidic Replacement of the PKC phosphorylation Site Ser-23", cited in the information disclosure statement filed on 09/28/2005 have been considered as part of the information disclosure statement filed on 12/12/2005

### ***Claim Objections***

3. Claim 5 is objected to because of the following informalities: Claim 5 recites the limitation "the synthesized protein fragments" which is not present prior to said

limitation. Suggested correction is to replace “the synthesized protein fragments” with “the protein fragments”. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 includes the use of an incomplete wherein clause rendering the claim indefinite because it is not clear how the recited “utilisation of protein fragments or polypeptides as sensors created from amino acid residues (moieties 1, 2) which possess a series of charged residues, and a recognition site containing modification residue(s) X and displaying a molecular electrostatic potential distribution” relate to the claimed method.

Claim 4 recites the limitation “the manufacturer” which is not recited prior to said limitation. Further, the phrase “as prescribed by the manufacturer” does not particularly point out what specific limitations are encompassed by said phrase and as such renders the claim indefinite.

Claim 8 recites an “Electronic system based on claim 1”. The phrase “electronic system based on claim 1” does not particularly point out how the device as claimed relates to the method of claim 1 and as such renders the claim indefinite.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (US 2003/0057968)

Regarding Claim 8 Wang et al. discloses an electronic system in which an integral part consists of measuring equipment (See [0034] and Fig. 7 where measuring equipment is sensor (103) integral to electronic system of Fig. 7) suitable for the supply of differential measurement results (See [0002]) which can calculate the difference in the alterations (See [0034]), to which if necessary a differential amplifier may be connected on the load side (See Fig. 7 110 and [0034]), followed by an alternating-current/direct-current converter. (See Fig. 2 114 and [0034])

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad (US 6,306,584) in view of Brandt et al. (Predicted Alterations in Tertiary Structure of the N- Terminus of the Na+/K+-ATPase  $\alpha$ -subunit Caused by Phosphorylation or Acidic Replacement or PKC Phosphorylation of Ser-23).

Regarding Claim 1 Bamdad discloses a method for the detection of posttranslational modification activities (See Bamdad C 22 L 3-8 where phosphorylation

is a posttranslational modification activity and is detected see C 22 L 34-45), wherein the utilisation of protein fragments or polypeptides as sensors (See Bamdad C 22 L 3-8 where chemically or biologically active species acts as a sensor), whereby the electrostatic potential distribution is measured as a dipole moment (See Bamdad C 22 L 27-63), enzymes are added to the sensor (See Bamdad C 22 L 15-18), the dipole moment is measured for a second time and a variation in the electrostatic potential and therefore dipole moment represents the detection of posttranslational modification activities. (See Bamdad C 22 L 27-63 where measuring a change in a property implies at least a first and second measurement)

Bamdad does not specifically teach protein fragments or polypeptides created from amino acid residues which possess a series of charged residues, and a recognition site containing modification residue(s) and displaying a molecular electrostatic potential distribution. The reference does not teach any method by which the protein fragments or polypeptides are created.

Brandt et al. teaches protein fragments or polypeptides created from amino acid residues which possess a series of charged residues, (See C 1 Pg. 84) and a recognition site containing modification residue(s) (See C 1 Pg. 84) and displaying a molecular electrostatic potential distribution. (See Abstract)

Bamdad and Brandt et al. are analogous because both references teach monitoring and measuring of changes as a result of phosphorylation of a protein. (See Bamdad C 22 L 3-8 and Brandt Abstract)

It would have been obvious to one of ordinary skill in the art at the time of invention to use the protein fragments or polypeptides created from amino acid residues which possess a series of charged residues, and a recognition site containing modification residue(s) and displaying a molecular electrostatic potential distribution of Brandt as the active species of Bamdad because doing so allows the active species to undergo the stated phosphorylation and other detectable changes. Furthermore while Bamdad teaches the detection of phosphorylation he does not specifically teach the specific structure of the proteins used. It would have been obvious to one of ordinary skill in the art to use proteins with the protein/amino acid structure of Brandt et al. because Brandt et al. teaches that such proteins/amino acid structures undergo the specific changes detected by the method of Bamdad.

Regarding claim 2 modified Bamdad discloses all the claim limitations as set forth above as well as the method in which amino acid residues are present in a quantity from 0 to n and possess a series of charged residues. (See Bamdad C 22 L 3-8 where proteins are inherently made of amino acids and as such must have a length from 0 to n on either side of the recognition site)

Regarding claim 3 modified Bamdad discloses all the claim limitations as set forth above as well as the method in which the recognition site in combination with the modification residue / modification residues represents a recognition group only permitting the conversion of the modification residue through the specific proteins kinase or phosphatase. (See Bambad C 22 L 3-8 where species engage in phosphorylation which is a specific action by protein kinase as evidenced by Brandt Abstract and Introduction)

Regarding claim 4 modified Bamdad discloses all the claim limitations as set forth above as well as the method in which the amino acid residues in combination with the recognition site and modification residue / modification residues display a three-dimensional structure with a distribution of molecular electrostatic potential (See Brandt Abstract where conformational change implies that a three dimensional structure exists) and molecular dipole moment as prescribed by the manufacturer. (See Bamdad C 22 L 52-62)

Regarding claim 5 modified Bamdad discloses all the claim limitations as set forth above as well as the method in which the synthesized protein fragments are either dissolved in a solution or placed on a solid body. (See Bamdad C 22 L 15-23 and Figs. 15-17)

Regarding claim 6 modified Bamdad discloses all the claim limitations as set forth above as well as the method in which a change in the molecular electrostatic potential distribution of the protein fragment as a consequence of posttranslational modification activities is measured (As evidenced by Brandt Abstract) by the conversion of the electrostatic potential distribution into a different physical measurement unit and is indicated as such, and in which the electrostatic potential distribution in the altered dimensions of the different physical measurement unit is measured and/or recorded. (See Bamdad C 22 L 34-45 and L 52-62 where change in electrostatic potential distribution is measured by a change in an electronic property, voltage, impedance, dipole creation etc., and thus is converted to a different physical unit)

Regarding claim 7 modified Bamdad discloses all the claim limitations as set forth above as well as the method in which posttranslational modification activities are determined on the basis of a differential capacitance measurement (See Bamdad C 26 L 24-34) through the measurement and/or recording of the changes as  $\Delta U$ . (See Bamdad C 22 L 34-45 and L 52-56). It is noted that capacitance and voltage are inversely proportional so conversion from one unit to the other would be obvious to one of ordinary skill in the art and could be carried out using well known mathematical formulas.

11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Newman (US 4,822,566) in view of Kell et al. (US 5,569,591).

Regarding claim 9 Newman discloses an electronic system in which changes resulting from modification activities (See Abstract and C 3 L 44-58) are converted by means of existing components into analogue physical measurement results (See Abstract and C 15 L 60-C 16 L 5)

Newman does not disclose a device in which components are connected on their load side with an analogue-to-digital converter for the purpose of digital evaluation.

Kell et al. discloses an electronic system for measuring changes resulting from biological activities (See Abstract and C 3 L 48-60) in which components are connected on their load side with an analogue-to-digital converter for the purpose of digital evaluation. (See C 10 L 15-32)

Newman and Kell et al. are analogous because both references teach systems for the detection of a change in biological materials, including protein and enzymatic activity, by monitoring a change in electronic properties of the system. (See Newman C 3 L 44-58, Kell C 1 L 14-19, and Kell C 3 L 48-60)

It would have been obvious to one of ordinary skill in the art at the time of invention to add an analogue-to-digital converter for the purpose of digital evaluation as taught by Kell to the electronic system of Newman because doing so improves the

efficiency of the electronic system by allowing a computer to perform a digital evaluation and efficiently record, and/or calculate changes that occur in the system. (See Kell C 6 L 55-59, C 7 L 22-27, and C 10 L 15-32)

***Conclusion***

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Andersson (US 5,504,430) discloses an electronic measuring system including AC/DC converter and A/D converter connected to a computer.

Stanbro (US 5,082,627) discloses an electronic measuring system for detecting changes in capacitance due to a change in molecular properties.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JONATHAN M. HURST whose telephone number is (571)270-7065. The examiner can normally be reached on Mon. - Thurs. 6:30-5:00; Every Fri. off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Basia Ridley can be reached on (571)272-1453. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. M. H./

Examiner, Art Unit 4153

/Basia Ridley/  
Supervisory Patent Examiner, Art Unit 4153